Chiral Metal Template Induced Asymmetric Synthesis of a Mixed Phosphine−Phosphine Oxide Ligand

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The asymmetric hydrophosphination reaction of 1,1-bis(diphenylphosphino)ethene and diphenylphosphine promoted by a chiral organopalladium(II) complex derived from (*S*)-*N*,*N*-dimethyl-1-(1-naphthyl)ethylamine proceeded stereoselectively to generate an equilibrium mixture of four diastereomeric triphosphine palladium(II) template products in a ratio of 17:5:3:2. Alternatively, the direct coordination of 1,1,2-tris(diphenylphosphino)ethane to the chiral organopalladium template generated the same equilibrium mixture of diastereomeric products with the same stereoselectivity. Subsequent asymmetric oxidation of the diastereomeric template products with hydrogen peroxide proceeded stereoselectively to generate four diastereomeric monooxidation products in the ratio of 14:3:3:1. The effects of solvent, temperature, and alternative oxidizing agents were also studied. The naphthylamine auxiliary was removed chemoselectively from the template products by treatment with concentrated hydrochloric acid to form an enantiomerically enriched mixture of the corresponding dichloro complexes, which upon subsequent repeated recrystallization gave the predominant enantiomeric complex in its optically pure form. Further ligand displacement of the enantiomerically pure dichloro complex with aqueous cyanide liberated the free mixed phosphine−phosphine oxide ligand in quantitative yield.

Introduction

Mixed phosphine−phosphine oxide ligands have been proven to be useful in metal catalysis and medicinal research.[1−3] The presence of both soft (phosphorus) and hard (oxygen) Lewis bases in a molecule enables the coordination to different types of metals. An important feature of mixed phosphine−phosphine oxide ligands is their ability to act as hemilabile ligands, which plays an important role in catalytic reactions. Generally such ligands are prepared by selective oxidation of polyphosphines or via synthesis involving separate phosphorus units coming together to form the mixed phosphine−phosphine oxide ligands.[1] Although selective monooxidation of chiral di- and triphosphines has been reported,[4] the synthesis of chiral mixed phosphine−phosphine oxide ligands via asymmetric oxidation of polyphosphines has not been developed.

Over the years, chiral cyclometalated-amine complexes have contributed significantly to many aspects of synthetic chemistry. These organometallic compounds have been used as resolving agents for chiral ligands,[5] clear and reliable references for the NMR assignment of unknown absolute configurations,[5g,6] chiral derivatizing agents (CDAs) for enantiomeric purity determination of chiral compounds,[7] efficient chiral catalysts for asymmetric Claisen rearrangements,[8] reaction promoters for the oxidative coupling between vinylphos-

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(1) Grushin, V. V. *Chem. Rev.* **2004**, *104*, 1629 and references therein.

(2) Berners-Price, S. J.; Norman, R. E.; Sadler, P. J. *J. Inorg. Biochem.* **1987**, *31*, 197.

(3) Debnath, A. K.; Radigan, L.; Jiang, S. *J. Med. Chem.* **1999**, *42*, 3203.

(4) (a) Grushin, V. V. *Organometallics* **2001**, *20*, 3950. (b) Faller, J. W.; Grimmond, B. J.; D'Alliessi, D. G. *J. Am. Chem. Soc.* **2001**, *123*, 2525. (c) Brunner, H.; Lautenschlager, H.-J.; König, W. A.; Krebber, R. *Chem. Ber.* **1990**, *123*, 847.

(5) (a) Wild, S. B. *Coord. Chem. Rev.* **1997**, *166*, 291 and references therein. (b) Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 7932. (c) Schmid, R.; Cereghetti, M.; Heiser, B.; Schönholzer, P.; Hansen, H. J. *Helv. Chim. Acta* **1988**, *71*, 897. (d) Alcock, N. W.; Brown, J. M.; Hulmes, D. I. *Tetrahedron: Asymmetry* **1993**, *4*, 743. (e) Dunina, V. V.; Golovan, E. B. *Tetrahedron: Asymmetry* **1995**, *6*, 2747. (f) Doucet, H.; Brown, J. M. *Tetrahedron: Asymmetry* **1997**, *8*, 3775. (g) Dunina, V. V.; Kuz'mina, L. G.; Rubina, M. Y.; Grishin, Y. K.; Veits, Y. A.; Kazakova, E. I. *Tetrahedron: Asymmetry* **1999**, *10*, 1483. (h) Bienewald, F.; Ricard, L.; Mercier, F.; Mathey, F. *Tetrahedron: Asymmetry* **1999**, *10*, 4701. (i) Albert, J.; Cadena, M.; Granell, J.; Muller, G.; Ordinas, J. I.; Panyella, D.; Puerta, C.; Sañudo, C.; Velerga, P. *Organometallics* **1999**, *18*, 3511.

(6) (a) Bookham, J. L.; McFarlane, W. *J. Chem. Soc., Chem. Commun.* **1993**, 1352. (b) Aw, B. H.; Selvaratnam, S.; Leung, P. H.; Rees, N. H.; McFarlane, W. *Tetrahedron: Asymmetry* **1996**, *7*, 1753. (c) Aw, B. H.; Hor, T. S. A.; Selvaratnam, S.; Mok, K. F.; White, A. J. P.; Williams, D. J.; Rees, N. H.; McFarlane, W.; Leung, P. H. *Inorg. Chem.* **1997**, *36*, 2138.

(7) (a) Kyba, E. P.; Rines, S. P. *J. Org. Chem.* **1982**, *47*, 4800. (b) Miyashita, A.; Karino, H.; Shimamura, J.; Chiba, T.; Nagano, K.; Nohira, H.; Takaya, H. *Chem. Lett.* **1989**, 1849. (c) Chooi, S. Y. M.; Leung, P. H.; Lim, C. C.; Mok, K. F.; Quek, G. H.; Sim, K. Y.; Tan, M. K. *Tetrahedron: Asymmetry* **1992**, *3*, 529. (d) López, C.; Bosque, R.; Sainz, D.; Solans, X.; Font-Bardía, M. *Organometallics* **1997**, *16*, 3261. (e) Dunina, V. V.; Kuz'mina, L. G.; Kazakova, M. Y.; Grishin, Y. K.; Veits, Y. A.; Kazakova, E. I. *Tetrahedron: Asymmetry* **1997**, *8*, 2537. (f) Böhm, A.; Hauck, T.; Beck, W. Z. *Naturforch., B* **1999**, *54*, 1360. (g) Böhm, A.; Seebach, D. *Helv. Chim. Acta* **2000**, *83*, 3262.

(8) (a) Hollis, T. K.; Overman, L. E. *J. Organomet. Chem.* **1999**, *576*, 290 and references therein. (b) Leung, P. H.; Ng, K. H.; Li, Y.; White, A. J. P.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1999**, 2435.

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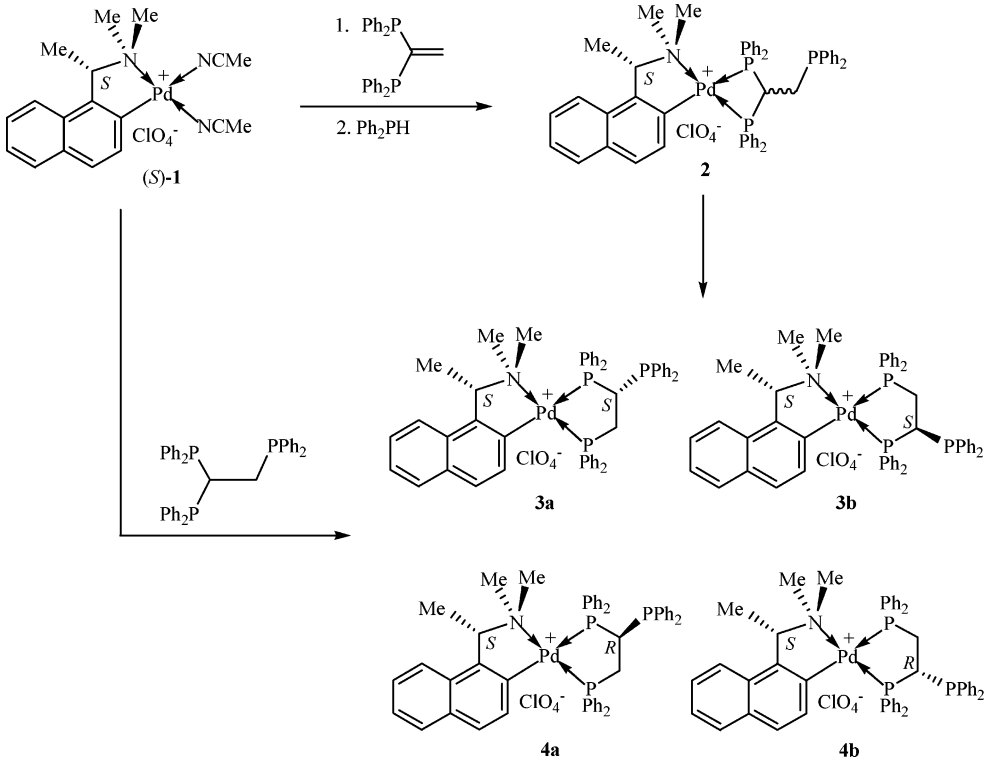
Scheme 1



phines and imines,[9] and chiral templates for asymmetric [4 + 2] and [2 + 2] cycloaddition reactions[10,11] and the asymmetric hydroamination[12] reaction. Recently, we have found that asymmetric hydrophosphination reactions between diphenylphosphine and vinylphosphines can also be promoted efficiently by a chiral cyclopalladated-amine complex for the generation of a chiral diphosphine ligand in high regio- and stereoselectivities under mild conditions.[13] In the present studies, the use of metal template promoted hydrophosphination reactions for the generation of 1,1,2-tris(diphenylphosphino)-ethane was investigated. Subsequent chiral metal template induced asymmetric monooxidation of the triphosphine ligand was demonstrated for the synthesis of a chiral mixed phosphine−phosphine oxide ligand.

Results and Discussion

It has been well established that, on coordination of 1,1-bis(diphenylphosphino)ethene to transition metals, the vinylidene double bond is particularly activated toward nucleophilic Michael addition with a wide range of nucleophiles such as amines, hydrazines, phosphines, carbanions, alcohols, thiols, and pyrrole.[14] Hence it is expected that metal activation of 1,1-bis(diphenylphosphino)ethene toward nucleophiles and chiral induction can be achieved with the use of the chiral cyclopalladated-amine complex (*S*)-**1**. Indeed, nucleophilic addition of diphenylphosphine to the chiral metal template activated 1,1-bis(diphenylphosphino)ethene proceeds smoothly at room temperature to give an equilibrium mixture of four diastereomeric products, as shown by ^{31}P NMR studies (Scheme 1). The ^{31}P NMR spectrum of the diastereomeric addition product mixture in $CDCl_3$ exhibited three sets of three doublet of doublets signals at δ [−14.7 ($^2J_{PP}$ = 19.1 Hz, $^3J_{PP}$ = 22.9 Hz), 47.5 (J_{PP} = 30.5 Hz, $^2J_{PP}$ = 19.1 Hz), and 55.9 (J_{PP} = 30.5 Hz, $^3J_{PP}$ = 22.9 Hz)], [−13.5 ($^2J_{PP}$ = 30.5 Hz, $^3J_{PP}$ = 11.4 Hz), 33.7 (J_{PP} = 34.3 Hz, $^3J_{PP}$ = 11.4 Hz) ,and 65.4 (J_{PP} = 34.3 Hz, $^2J_{PP}$ = 30.5 Hz)], and [−16.9 ($^2J_{PP}$ = 72.5 Hz, $^3J_{PP}$ = 7.6 Hz), 39.0 (J_{PP} = 26.7 Hz, $^3J_{PP}$ = 7.6 Hz), and 73.2 (J_{PP} = 26.7 Hz, $^2J_{PP}$ = 72.5 Hz)], together with a set of two doublet of doublets and a triplet resonance signal at [48.5 (J_{PP} = 30.5 Hz, $^2J_{PP}$ = 22.9 Hz), 55.5 (J_{PP} = 30.5 Hz, $^3J_{PP}$ = 22.9 Hz), and −14.3 ($^2J_{PP}$ = $^3J_{PP}$ = 22.9 Hz)] in an equilibrium ratio of 17:5:2:3, respectively. The stereoselectivity of the reaction is not affected by solvent effects. When the reaction is performed in various solvents (dichloromethane, chloroform, acetonitrile, methanol, benzene) and monitored by ^{31}P NMR with their respective deuterated solvents, similar product selectivity was obtained. From the ^{31}P NMR data, it is obvious that two of the phosphorus atoms are

(9) Liu, X. M.; Mok, K. F.; Vittal, J. J.; Leung, P. H. *Organometallics* **2000**, *19*, 3722.

(10) (a) Leung, P. H. *Acc. Chem. Res.* **2004**, *37*, 169 and references therein. (b) Yeo, W. C.; Vittal, J. J.; White, A. J. P.; Williams, D. J.; Leung, P. H. *Organometallics* **2001**, *20*, 2167. (c) Yeo, W. C.; Vittal, J. J.; Koh, L. L.; Tan, G. K.; Leung, P. H. *Organometallics* **2004**, *23*, 3474.

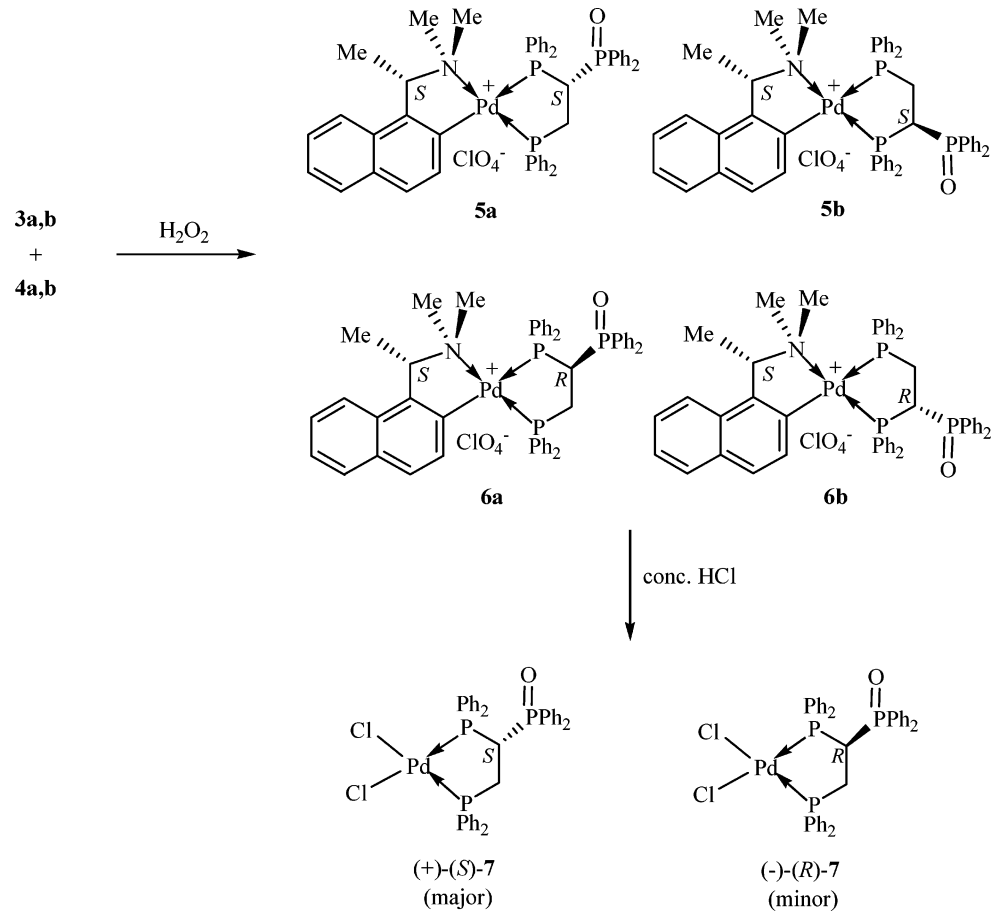
(11) Yeo, W. C.; Tan, G. K.; Koh, L. L.; Leung, P. H. *Eur. J. Inorg. Chem.* accepted.

(12) Liu, X. M.; Mok, K. F.; Leung, P. H. *Organometallics* **2001**, *20*, 3918.

(13) Yeo, W. C.; Tee, S. Y.; Tan, H. B.; Tan, G. K.; Koh, L. L.; Leung, P. H. *Inorg. Chem.* **2004**, *43*, 8102.

(14) (a) Cooper, G. R.; Hassan, F.; Shaw, B. L.; Thornton-Pett, M. *J. Chem. Soc., Chem. Commun.* **1985**, 614. (b) Cooper, G. R.; McEwan, D. M.; Shaw, B. L. *Inorg. Chim. Acta* **1986**, *122*, 207. (c) Herring, A. M.; Higgins, S. J.; Jacobsen, G. B.; Shaw, B. L. *J. Chem. Soc., Chem. Commun.* **1986**, 882. (d) Hassan, F. S. M.; Higgins, S. J.; Jacobsen, G. B.; Shaw, B. L.; Thornton-Pett, M. *J. Chem. Soc., Dalton Trans.* **1988**, 3011. (e) Higgins, S. J.; Shaw, B. L. *J. Chem. Soc., Dalton Trans.* **1989**, 1527. (f) Dolby, P. A.; Harding, M. M.; Newar, N.; Smith, A. K. *J. Chem. Soc., Dalton Trans.* **1992**, 2939. (g) King, G.; Higgins, S. J.; Hopton, A. *J. Chem. Soc., Dalton Trans.* **1992**, 3403. (h) Fernández, E. J.; Gimeno, M. C.; Jones, P. G.; Laguna, A.; Olmos, E. *Organometallics* **1997**, *16*, 1130. (i) Barkley, J. V.; Higgins, S. J.; McCart, M. K.; Pounds, T. J. *Inorg. Chem.* **1997**, *36*, 6188.

Scheme 2



coordinated to the metal, while the remaining phosphorus atom is in the uncoordinated form. The downfield resonances of the two coordinated phosphorus atoms with large coordination chemical shift is supportive of the formation of the five-membered chelation complexes **3a**,**b** and **4a**,**b**.[15] Nucleophilic addition of diphenylphosphine to the chiral metal template activated vinylidene double bond is believed to proceed with the initial generation of complex **2**, which subsequently undergoes facile rearrangement to the less strained five-membered-ring complexes **3a**,**b** and **4a**,**b**, which were the only products observed from the ^{31}P NMR studies.[14d] Further isomerization among complexes **3a**,**b** and **4a**,**b** was observed until an equilibrium was attained after 1 day at room temperature, and such isomerization would most probably proceed via complex **2** or five-coordinate palladium(II) intermediates.[16] As the ratio of the diastereomeric products obtained is determined by their thermodynamic stability due to the facile exchange of the diphenylphosphino groups, complexes **3a**,**b** and **4a**,**b** were alternatively formed in the same diastereomeric ratio by the direct coordination of the triphosphine ligand 1,1,2-tris(diphenylphosphino)ethane to the chiral metal complex (*S*)-**1** (Scheme 1).

It is noteworthy that the triphosphine ligand in complexes **3a**,**b** and **4a**,**b** is not chiral upon liberation from the chiral metal template. Since there is precedence in the literature for the oxidation of coordinated or uncoordinated phosphino groups in phosphine metal complexes,[1,4,17] chiral metal template induced stereoselective oxidation of complexes **3a**,**b** and **4a**,**b** was attempted with the aim of obtaining a chiral mixed phosphine−phosphine oxide ligand. Treatment of the mixture of complexes **3a**,**b** and **4a**,**b** with hydrogen peroxide generated four diastereomeric monooxidation products in a ratio of 14:3:3:1, as indicated by ^{31}P NMR studies (Scheme 2). Purification of these oxidation products by fractional crystallization was unsuccessful. Although the most predominant diastereomer could be obtained in relatively pure form by silica column chromatography, the isolation process was inefficient and resulted in low yields. Therefore, the crude diastereomeric product mixture was treated directly with concentrated hydrochloric acid for the chemoselective removal of the naphthylamine auxiliary, to generate an enantiomerically enriched mixture of dichloro complexes **7** (enriched in (+)-(*S*)-**7**). After repeated recrystallization, the neutral dichloro complex (+)-(*S*)-**7** was isolated in its enantiomerically pure form as colorless crystals in 40% yield, with $[\alpha]_D = +89°$ (CH_2Cl_2). The ^{31}P NMR spectrum of this crystallized product in CD_2Cl_2 exhibited three doublet of doublets resonance signals at δ [24.6

(15) Garrou, P. E. *Chem. Rev.* **1981**, *81*, 229.
(16) (a) Tau, K. D.; Uriarte, R.; Mazanec, T. J.; Meek, D. W. *J. Am. Chem. Soc.* **1979**, *101*, 6614. (b) Meek, D. W.; Mazanec, T. J. *Acc. Chem. Res.* **1981**, *14*, 266.

(17) (a) Sevillano, P.; Habtemariam, A.; Castiñeiras, A.; García, M. E.; Sadler, P. J. *Polyhedron* **1999**, *18*, 383. (b) Annibale, G.; Bergamini, P.; Bertolasi, V.; Besco, E.; Cattabriga, M.; Rossi, R. *Inorg. Chim. Acta* **2002**, *333*, 116. (c) Bianchini, C.; Meli, A.; Scapacci, G. *Organometallics* **1985**, *4*, 264. (d) Brandt, K.; Sheldrick, W. S. *Chem. Ber.* **1996**, *129*, 1199. (e) Heinze, K.; Huttner, G.; Zsolnai, L. *Chem. Ber./Recl.* **1997**, *130*, 1393.

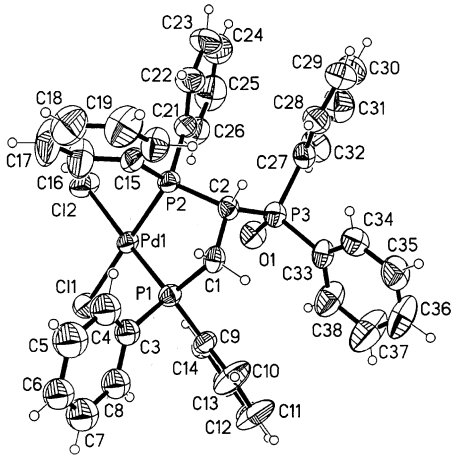


Figure 1. Molecular structure of the dichloro complex (+)-(*S*)-**7**.

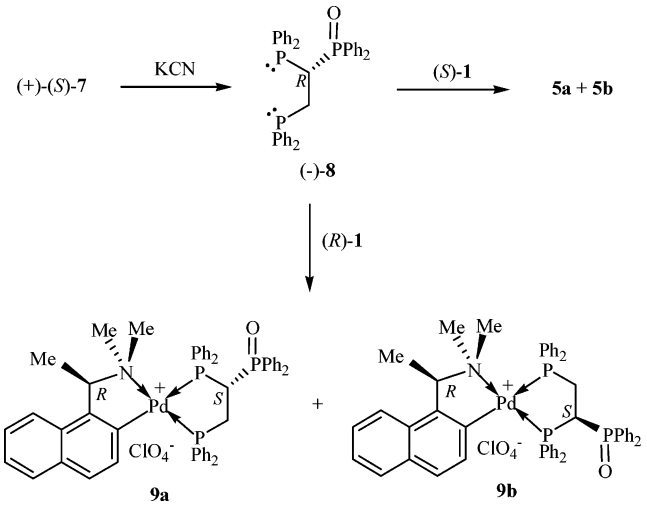
Table 1. Selected Bond Lengths (Å) and Angles (deg) for the Dichloro Complex (+)-(*S*)-7

Pd(1)−P(1)	2.241(1)	P(2)−C(2)	1.869(4)
Pd(1)−P(2)	2.235(1)	P(3)−C(2)	1.828(4)
Pd(1)−Cl(1)	2.348(1)	P(3)−O(1)	1.484(3)
Pd(1)−Cl(2)	2.364(1)	C(1)−C(2)	1.522(6)
P(1)−C(1)	1.845(4)		
P(1)−Pd(1)−Cl(1)	92.41(4)	Pd(1)−P(2)−C(2)	108.9(1)
P(1)−Pd(1)−Cl(2)	174.30(5)	P(1)−C(1)−C(2)	112.1(3)
P(1)−Pd(1)−P(2)	84.72(4)	P(2)−C(2)−C(1)	105.4(3)
P(2)−Pd(1)−Cl(1)	175.92(5)	P(2)−C(2)−P(3)	112.8(2)
P(2)−Pd(1)−Cl(2)	91.45(4)	C(1)−C(2)−P(3)	113.5(3)
Pd(1)−P(1)−C(1)	109.8(1)		

($^2J_{PP}$ = 21.0 Hz, $^3J_{PP}$ = 66.8 Hz), 55.2 (J_{PP} = 11.4 Hz, $^3J_{PP}$ = 66.8 Hz), and 70.4 (J_{PP} = 11.4 Hz, $^2J_{PP}$ = 21.0 Hz)]. The molecular structure and absolute configuration of (+)-(*S*)-**7** were subsequently confirmed by X-ray crystallography (Figure 1). Selected bond lengths and angles are given in Table 1. The structural analysis affirmed that a five-membered diphosphine chelate with a dangling diphenylphosphinyl group was formed, and the stereogenic center at C(2) is established to adopt the *S* absolute configuration.

Further treatment of (+)-(*S*)-**7** with aqueous cyanide liberated the optically pure mixed phosphine−phosphine oxide ligand (−)-**8** as a white solid in quantitative yield, with $[\alpha]_D = -45°$ ($CHCl_3$) (Scheme 3). The ^{31}P NMR spectrum of this free ligand showed three doublet of doublets at [δ 34.6 ($^2J_{PP}$ = 76.3 Hz, $^3J_{PP}$ = 26.7 Hz), −8.8 ($^2J_{PP}$ = 76.3 Hz, $^3J_{PP}$ = 7.6 Hz), and −16.7 ($^3J_{PP}$ = 7.6 Hz, $^3J_{PP}$ = 26.7 Hz)]. The optical purity of (−)-**8** (i.e., also the dichloro complex (+)-(*S*)-**7**) was confirmed by recoordination of the free ligand to (*S*)-**1** and the equally available enantiomeric complex (*R*)-**1** separately. Recomplexation of (−)-**8** to (*S*)-**1** gave only the pair of regioisomers **5a**,**b** (Scheme 3), which was found to undergo cis−trans isomerization in solution until an equilibrium between the two cis−trans isomers was achieved.[13,18] The ^{31}P NMR spectrum of the recomplexation product mixture in $CDCl_3$ exhibited two sets of resonance signals, each consisting of three doublet of doublets signals at δ [26.9 ($^3J_{PP}$ = 53.4 Hz, $^2J_{PP}$ = 22.9 Hz), 43.8 (J_{PP} = 34.3 Hz, $^2J_{PP}$ = 22.9 Hz), and 53.5 (J_{PP} = 34.3 Hz, $^3J_{PP}$ = 53.4 Hz)] and [28.1 ($^3J_{PP}$ = 42.0 Hz, $^2J_{PP}$ = 15.3 Hz), 34.8 (J_{PP} = 34.3 Hz, $^3J_{PP}$ = 42.0 Hz), and 67.9 (J_{PP} = 34.3 Hz, $^2J_{PP}$ = 15.3 Hz)] in an equilibrium ratio of 5:1, respectively. It is noteworthy that the phosphorus resonance signals for these two regioisomeric recomplexation products are identical with those recorded for the most predominant and one of the diastereomeric products (with relative abundance of 3) in the 14:3:3:1 product mixture obtained directly from the asymmetric oxidation reaction. Recoordination of (−)-**8** to (*R*)-**1** similarly generated only the pair of regioisomeric complexes **9a**,**b** (Scheme 3), which are the enantiomeric forms of **6a**,**b**, respectively. The ^{31}P NMR spectrum of the recomplexation product mixture in $CDCl_3$ showed a set of three doublet of doublets signals at δ [28.7 ($^3J_{PP}$ = 34.3 Hz, $^2J_{PP}$ = 15.3 Hz), 45.7 (J_{PP} = 30.5 Hz, $^2J_{PP}$ = 15.3 Hz) and 55.0 (J_{PP} = 30.5 Hz, $^3J_{PP}$ = 34.3 Hz)], together with a set of two doublets and a singlet phosphorus resonance signal at δ [40.6 (J_{PP} = 26.7 Hz), 72.8 (J_{PP} = 26.7 Hz), and 30.2] in an equilibrium ratio of 1:3, respectively. It is noteworthy that the resonance signals for the two recomplexation products are identical with those recorded for the other two remaining diastereomeric products obtained directly from the asymmetric oxidation reaction. Importantly, since the phosphorus resonance signals corresponding to complexes **5a**,**b** were not observed, this confirmed the optical purity of the mixed phosphine−phosphine oxide ligand (−)-**8** (and also (+)-(*S*)-**7**). From these recoordination experiments and spectroscopic and crystallographic studies, the four stereoisomeric products generated in the chiral metal template induced asymmetric oxidation of 1,1,2-tris(diphenylphosphino)ethane have been established to be complexes **5a**,**b** and **6a**,**b**.

Scheme 3



The solvent and temperature effects on the stereoselectivity of the asymmetric oxidation step have been studied. The use of various solvents (dichloromethane, chloroform, acetonitrile, methanol) and temperatures (−5, 25, 40, 61 °C) has little effect on the stereoselectivity, as there is no significant changes, with only minor variations in the product selectivity. Oxidation of complexes **3a**,**b** and **4a**,**b** has also been attempted with other oxidizing agents. When *tert*-butyl hydroperoxide instead of hydrogen peroxide was used as the oxidizing agent, comparable stereoselectivities were obtained. Oxidation with oxygen gas has been found to proceed very slowly; only about 5% of the oxidized product was formed after

(18) Leitch, J.; Salem, G.; Hockless, D. C. R. *J. Chem. Soc., Dalton Trans.* **1995**, 649.

2 days at room temperature. The use of potassium permanganate or iodine as the oxidant has resulted in the formation of a complex mixture of unidentified compounds predominantly.

In conclusion, two converging synthetic pathways sharing a common metal template induced asymmetric oxidation process have been illustrated for the synthesis of chiral phosphine−phosphine oxide ligands. The common intermediates, 1,1,2-tris(diphenylphosphino)ethane palladium(II) template complexes, were formed as an equilibrium diastereomeric mixture, due to the facile exchange of the diphenylphosphino groups of the metal-coordinated triphosphine ligand. Further investigations on the synthesis of P-stereogenic mixed phosphine−phosphine oxide ligands and the applicability of other oxidation processes are currently in progress.

Experimental Section

Reactions involving air-sensitive compounds were performed under a positive pressure of purified nitrogen. NMR spectra were recorded at 25 °C on Bruker ACF 300 and AMX500 spectrometers. The spectral assignments in the ^{31}P and ^{1}H NMR spectra are based on selective decoupling of the three types of ^{31}P nuclei and NOE data from the 2D $^{1}H-^{1}H$ ROESY spectrum.[6b] The phase-sensitive ROESY NMR experiment was acquired into a 1024 × 512 matrix with a 250 ms spin locking time and a spin lock field strength such that $\gamma B_1/2\pi = 5000$ Hz and then transformed into 1024 × 1024 points using a sine bell weighting function in both dimensions. Optical rotations were measured on the specified solution in a 0.1 dm cell at 25 °C with a Perkin-Elmer Model 341 polarimeter. Melting points were determined on a Büchi melting point B-540 apparatus. Elemental analysis was performed by the Elemental Analysis Laboratory of the Department of Chemistry at the National University of Singapore.

The enantiomerically pure forms of (*S*)-**1** and (*R*)-**1** were prepared according to the literature method.[19] 1,1-Bis(diphenylphosphino)ethene was purchased from Aldrich Chemical Co. and used directly.

Caution! *All perchlorate salts should be handled as potentially explosive compounds.*

Asymmetric Oxidation Reaction and Removal of the Naphthylamine Auxiliary. Isolation of [*SP*-4-3-(*S*)-Dichloro{1-diphenylphosphinyl-1,2-bis(diphenylphosphino)ethane-*P*^{1},*P*^{2}}]palladium(II) ((+)-(*S*)-7). The triphosphine ligand 1,1,2-tris(diphenylphosphino)ethane was synthesized by refluxing 1,1-bis(diphenylphosphino)ethene (0.616 g), diphenylphosphine (0.289 g), and a catalytic amount of potassium *tert*-butoxide in THF (25 mL) for 2 h.[20] After that the mixture was added to a solution of (*S*)-**1** (0.748 g) in dichloromethane (20 mL) and stirred at room temperature for 1 day. Aqueous hydrogen peroxide solution (30%, 10 mL) was added and the mixture stirred vigorously for 1 h. The solvents were removed, the reaction mixture was redissolved in dichloromethane (50 mL), and this solution was then subsequently washed with water (3 × 40 mL). Concentrated hydrochloric acid (15 mL) was added to the solution and the mixture stirred vigorously for 16 h. The mixture was washed with water (3 × 40 mL) and dried ($MgSO_4$). After repeated recrystallization from dichloromethane−diethyl ether, optically pure (+)-(*S*)-**7** was obtained as colorless crystals: mp 331−333 °C dec; $[\alpha]_D = +89°$ (*c* 0.1, CH_2Cl_2); 0.473 g (40% yield). Anal. Calcd for $C_{38}H_{33}Cl_2OP_3Pd$: C, 58.8; H, 4.3. Found: C, 58.5; H, 4.2. ^{31}P NMR (CD_2Cl_2): δ 24.6 (dd, 1P, $^{2}J_{PP} = 21.0$ Hz, $^{3}J_{PP} = 66.8$ Hz, P_3), 55.2 (dd, 1P, $J_{PP} = 11.4$ Hz, $^{3}J_{PP} = 66.8$ Hz, P_2), 70.4 (dd, 1P, $J_{PP} = 11.4$ Hz, $^{2}J_{PP} = 21.0$ Hz, P_1). ^{1}H NMR (CD_2Cl_2): δ 2.51−2.93 (m, 2H, H_2, $H_{2'}$), 3.03−3.22 (m, 1H, H_1), 7.04−8.43 (m, 30H, aromatics).

Table 2. Crystallographic Data for the Dichloro Complex (+)-(*S*)-7

formula	$C_{38}H_{33}Cl_2OP_3Pd$
fw	775.85
space group	$P2_12_12_1$
cryst syst	orthorhombic
a/Å	8.2326(8)
b/Å	20.152(2)
c/Å	20.929(2)
V/Å^3	3472.3(6)
Z	4
T/K	295(2)
ρ_{calcd}/g cm^{-3}	1.484
λ/Å	0.71073 (Mo)
μ/cm^{-1}	8.57
Flack param	0.01(3)
R1 (obsd data)[a]	0.0479
wR2 (obsd data)[b]	0.0995

[a] $R1 = \sum||F_o| - |F_c||/\sum|F_o|$. [b] $wR2 = \{\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]\}^{1/2}$; $w^{-1} = \sigma^2(F_o^2) + (aP)^2 + bP$.

Procedure for the Nucleophilic Addition−Asymmetric Oxidation Pathway. Stoichiometric amounts of complex (*S*)-**1**, 1,1-bis(diphenylphosphino)ethene, and diphenylphosphine were stirred in dichloromethane at room temperature for 1 day. Subsequent asymmetric oxidation and removal of the naphthylamine auxiliary were performed as described earlier.

Liberation of (*R*)-1-(Diphenylphosphinyl)-1,2-bis(diphenylphosphino)ethane ((−)-8). A solution of (+)-(*S*)-**7** (0.072 g) in dichloromethane (30 mL) was stirred vigorously with a saturated aqueous solution of potassium cyanide (2 g) for 2 h. The organic layer was separated, washed with water (3 × 20 mL), and dried ($MgSO_4$). Upon removal of the solvent, a white solid was obtained: $[\alpha]_D = -45°$ (*c* 0.7, $CHCl_3$); 0.053 g (95% yield). ^{31}P NMR ($CDCl_3$): δ 34.6 (dd, 1P, $^{2}J_{PP} = 76.3$ Hz, $^{3}J_{PP} = 26.7$ Hz, P_1), −8.8 (dd, 1P, $^{2}J_{PP} = 76.3$ Hz, $^{3}J_{PP} = 7.6$ Hz, P_2), −16.7 (dd, 1P, $^{3}J_{PP} = 7.6$ Hz, $^{3}J_{PP} = 26.7$ Hz, P_3). ^{1}H NMR ($CDCl_3$): δ 2.06−2.22 (m, 1H, H_2), 2.51−2.69 (m, 1H, $H_{2'}$), 3.02−3.18 (m, 1H, H_1), 6.62−7.72 (m, 30H, aromatics).

Typical Procedure Used for the Recomplexation Reactions. Stoichiometric amounts of complexes (*S*)-**1** and (−)-**8** were stirred in dichloromethane at room temperature.

Crystal Structure Determination of (+)-(*S*)-7. X-ray crystallographic data for the complex (+)-(*S*)-**7** are given in Table 2. The structure was analyzed at the National University of Singapore using a Siemens SMART CCD diffractometer with graphic-monochromated Mo Kα radiation. SADABS absorption correction was applied. One of the phenyl rings, C(3)−C(8), is disordered into two positions with occupancies of 60/40, respectively. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were introduced at a fixed distance from carbon atoms and were assigned fixed thermal parameters. The absolute configuration of (+)-(*S*)-**7** was determined unambiguously using the Flack parameter.[21]

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Supporting Information Available: For the complex (+)-(*S*)-**7**, a CIF file giving X-ray crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(19) Chooi, S. Y. M.; Leung, P. H.; Lim, C. C.; Mok, K. F.; Quek, G. H.; Sim, K. Y.; Tan, M. K. *Tetrahedron: Asymmetry* **1992**, *3*, 529.

(20) Bookham, J. L.; McFarlane, W. *J. Chem. Soc., Dalton Trans.* **1988**, 503.

(21) Flack, H. D. *Acta Crystallogr.* **1983**, *A39*, 876.